Answer 1:

Bibliographic Information

Reversal of the human and murine multidrug-resistance phenotype with megestrol acetate. Wang, Lotte; Yang, Chia-Ping H.; Horwitz, Susan Band; Trail, Pamela A.; Casazza, Anna M. Pharmaceutical Research Institute, Bristol-Myers Squibb Company, Princeton, NJ, USA. Cancer Chemotherapy and Pharmacology (1994), 34(2), 96-102. CODEN: CCPHDZ ISSN: 0344-5704. Journal written in English. CAN 121:169967 AN 1994:569967 CAPLUS

Abstract

Megesterol acetate (MA) is an orally active progesterone (PG) deriv. with an excellent safety profile that is used primarily for the treatment of carcinomas of the breast and endometrium. We investigated the potential application of MA as an MDR-reversal agent using cell culture and human tumor xenograft models. The reversing activity of MA in vitro was compared with that of PG and verapamil (VER) in two human MDR cell lines, the colon carcinoma HCT-116/VM46 and the breast carcinoma MCF-7/ADR, and in a murine cell line, J774.2. At concns. as low as 3 μM, MA was capable of partially restoring sensitivity to actinomycin D (Act D) in the HCT-116/VM46 cells and sensitivity to doxorubicin (DOX) in the MCF-7/ADR cells. Although less effective than VER, MA was about 2.5 times more potent than PG in reversing MDR at equimolar concns. Increased accumulation of DOX in drug-resistant cells that were treated simultaneously with MA was obsd. by flow cytometry. In vivo, using established human colon and breast carcinoma xenografts implanted s.c. in athymic mice, the combined therapy with MA and DOX resulted in enhanced antitumor activity relative to that of DOX alone in the MDR sublines. These results suggest that MA may be a promising clin. MDR-reversing agent.